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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,105	05/02/2007	Dan H Barouch	01948/098003	4894

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/09/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/580,105	BAROUCH ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/19/06, 12/7/09, 9/30/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-9,12, 15-17, 19-38, 40-44, 46-53, 56-64* is/are pending in the application.

4a) Of the above claim(s) *23,24,29-38,44,46-53 and 56-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-9,12,15-17,19-22,25-28 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 5/19/06 and Applicant's responses filed 12/7/09 and 9/30/10 are acknowledged and have been entered.

2. Applicant's election of Group II without traverse in Applicant's response filed 12/7/09 and Applicant's election without traverse of the species env for both immunogen and antigen, and MIP-1α, HIV as the condition to be treated and GM-CSF as the adjuvant in Applicant's response filed 9/30/10 is acknowledged.

Claims 1, 5, 7-9, 12, 15-16, 19-22, 25-28 and 40-43 read on the elected species.

Upon consideration of the prior art, examination has been extended to include the species recited in instant claim 17.

Accordingly, claims 23, 24, 29-38, 44, 46-53, 56-62 and 64 (non-elected groups) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Applicant is reminded that base claim 1 contains limitations that belong to non-elected groups, *i.e.,* at part "(ii)".

Claims 1, 5, 7-9, 12, 15-17, 19-22, 25-28 and 40-43 are currently being examined as they read on the administration of polypeptides, not nucleic acid molecules.

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has claimed a method of enhancing the immune response to an immunogen in a mammal by administering said immunogen, Flt3L. or a biologically active fragment thereof and MIP-1α or MIP-3α or a biologically active fragment thereof, wherein said method is used to treat or prevent any microbial infection (claim 27) including HIV

infection (claim 28), using an immunogen that is "substantially identical to an antigen associated with said microbial infection."

The specification does not disclose a definition for "substantially identical" to an "antigen associated with" a microbial infection. Nor does the specification disclose a representative number of species of such immunogen. Nor does the specification provide a structure/function relationship for what makes the immunogen of the claimed method "substantially identical" to an antigen associated with a microbial infection, and sufficient to confer the functional outcome of "enhancing an immune response."

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106 column 3).

The court has further stated that "Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

In light of this, a skilled artisan would reasonably conclude that Applicant was not in possession of claimed invention at the time the instant application was filed.

6. Claims 20-22 and 25-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and use the instant invention, a method of enhancing the immune response to an immunogen in a mammal by administering said immunogen, Flt3L. or a biologically active fragment thereof and MIP-1α or MIP-3α or a biologically active fragment thereof, wherein the mammal is a neonate (claims 20 and 21) and said method is to prevent viral transmission during breastfeeding (claim 21), or wherein said method is used to treat or prevent any microbial infection (claims 22, 25 and 27) including HIV infection (claims 26 and 28), including other recited limitations.

The specification has not enabled the breadth of the claimed invention because the claims encompass enhancing an immune response to an immunogen in a neonate which neonate does not have a developed immune system to mount an immune response, nor an enhanced immune response, and further also encompasses preventing HIV or other viral transmission during breastfeeding (claims 20 and 21), or because the claims encompass treating or preventing any microbial infection, including HIV, by administering an immunogen(s) (claims 22 and 25-28), wherein said administration may not treat or prevent the infection, and wherein the other recited components are adjuvants.

The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed method can be used for the recited purposes.

The specification discloses no working examples with regards to treating a neonate or preventing viral transmission during breastfeeding, nor of treating or preventing any microbial infection, including HIV.

The specification discloses that antigen-specific T cells may be amplified *in vivo* when an immunogen, Flt3L and MIP-1α or MIP-3α -encoding nucleic acid molecules comprised in vectors are administered to mice (for example, Figures 4-13 as well as the brief description of the drawings for these Figures). The specification discloses treatment or prevention of microbial infections in a prophetic manner (for example, page 21 at lines 10-29, page 22 at lines 1-3). The specification further discloses that "Without wishing to be bound by any particular mechanism, we believe that plasmid MIP-1α and Flt3L function by exerting local effects and in particular by recruiting, expanding, and activating DCs at the site of innoculation and antigen production." (page 40 at lines 22-25).

Evidentiary reference Falcao teaches that a newborn does not yet have a mature immune system and is often unable to mount an effective immune response (particularly first sentence of reference).

Evidentiary reference Marodi (Haematologica Reports 2006, 2(10): 6-8) teaches that neonatal monocytes and macrophages are qualitatively different from adult cells in their defective secretion of a variety of Th1-type cytokines, innate immune cells such as monocytes and macrophages, and an overall neonatal defect of receptor-mediated signaling and stimulus-response coupling (especially last paragraph of reference).

In addition, it is well known in the art that retroviral therapies, especially HIV therapies, are refractory to anti-viral therapies (see Fahey *et al.*, Clinical Experimental Immunology, 1992; Letvin, Science, 1998). The obstacles to developing a successful therapy of HIV are well documented in the literature. These obstacles include 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with the respect to the gene encoding the envelope protein. 2) The fact that

the mode of viral transmission includes both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission. 3) The establishment of a latent viral infection. 4) The ability of the virus to evade the immune responses in the central nervous system due to the blood-brain barrier. 5) The complexity and variation of the pathology of HIV infection in different individuals. 6) The inability of a natural infection to one strain of HIV to protect an individual from being infected with another strain of HIV (Machuca *et al.* Intervirology 1999, see discussion). These obstacles establish that the contemporary knowledge in the art would not allow one of skill in the art to use the claimed vaccine to treat and/or prevent HIV infection without undue experimentation. Furthermore, it is well known in the art that individuals infected with HIV produce neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion.

Applicants have not provided any convincing evidence that their claimed method is indeed useful as a therapeutic or preventative for HIV infection or for any other infection, including in a neonate, and have not provided sufficient guidance in to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence in light of the high degree of unpredictability in the art regarding which structural features are required in order to provide treatment or protection, the absence of working examples directed to the same, the complex nature of the invention, the specification fails to provide an enabling disclosure.

There is insufficient guidance in the specification as to how to use the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1, 5, 7-9, 12, 15-17, 19-22, 25-28 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,933,377 B2.

Applicant is reminded that "what constitutes proper enablement of a prior art reference for purposes of anticipation under section 102...differs from the enablement standard

under section 112." Rasmusson v. Smithkline Beechan Corp., Case Nos. 04-1192 (Fed. Cir. June 27, 2005)

US 6,933,377 B2 discloses treating and preventing HIV by administering an HIV gene product(s) wherein the administering includes administering one or more adjuvants that is/are a co-stimulatory molecule, a cytokine, a chemokine and a growth factor. US 6,933,377 B2 discloses that these adjuvants may include Flt3 ligand, GM-CSF growth factor and chemokine MIP-1α, and the route of administration is preferably IM, IV, IP and SC. US 6,933,377 B2 discloses that the env, pol and/or gag gene products are immunogens that can be used in the method. US 6,933,377 B2 further discloses that the administering may be to a neonate, a child, an adolescent or an adult human, nonhuman primate, cow, horse, sheep, rodent, goat or cat, and that the providing step may be one administration or multiple administrations. US 6,933,377 B2 discloses that the immune response may be a CTL and/or Th response (*i.e.,* a CD8+ T cell and/or CD4+ T cell response, respectively) (especially abstract, column 1 at lines 55-67, column 2 at lines 1-29, column 3 at lines 19-23, Tables 1 and 2, column 16 at lines 64-67, column 17 at lines 1-10, column 20 at lines 65-67, column 21 at lines 1, 40-49).

With regard to the inclusion of instant claims 7 and 8 in this rejection, although the art reference does not teach the % T cell response augmentation, the method steps taught by the art are the same method steps recited in the instant claim.

As per MPEP 2111.04, claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

(A) "adapted to" or "adapted for" clauses;
(B) "wherein" clauses; and
(C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In Hoffer v. Microsoft Corp., 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "'whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recited "wherein" clause (claims 7 and 8) simply expresses the intended result that occurs upon performing the method steps.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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